



Attorney Docket 1087(A1-35US3)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: ROBERT J. LIPSHUTZ et al.
Serial No.: 09/519,148
Filed : March 6, 2000

Art Unit : 1655
Examiner : Bradley L. Sisson

Title: INTEGRATED NUCLEIC ACID DIAGNOSTIC DEVICE

ALL PENDING CLAIMS

80. A method of analyzing a sample in an integrated microfluidic device having at least two chambers in fluid communication, comprising:

supplying the sample into a first chamber of the integrated microfluidic device, wherein the first chamber is selected from the group of chambers adapted to perform a preparative reaction, an analysis reaction, sample acquisition, DNA extraction, amplification, IV transcription or labeling;

performing a first reaction in the first chamber;

moving the sample from the first chamber to the second chamber, wherein the second chamber is selected from the group of chambers adapted to perform a preparative reaction, an analysis reaction, sample acquisition, DNA extraction, amplification, IV transcription or labeling;

performing a second reaction in the second chamber, the second reaction being different from the first reaction;

performing confocal microscopy using a reader device;

receiving a signal output from the reader device; and

analyzing the signal output with a digital computer to indicate a property of the sample.

81. The method of claim 80, wherein the preparative reaction comprises:

a reaction selected from the group of reactions consisting of sample extraction, PCR amplification, extraction of intracellular material, nucleic acid fragmentation, labeling, extension reactions and transcription reactions.

82. The method of claim 80, wherein the analysis reaction comprises:
a reaction selected from the group of reactions consisting of size based analysis or sequence based analysis.

83. The method of claim 82, wherein size based analysis comprises microcapillary electrophoresis.

84. The method of claim 82, wherein sequence based analysis comprises hybridization of targets to a nucleic acid array.

85. The method of claim 80, wherein the sample acquisition comprises:
a reaction selected from the group of reactions consisting of neutralizing an infectious agent or performing a pH adjustment.

86. The method of claim 85, wherein neutralizing an infectious agent comprises introduction of heparin, buffering agents, protease or nuclease inhibitors or preservatives.

87. The method of claim 80, wherein DNA extraction comprises:
a reaction for extracting DNA selected from the group of reactions consisting of denaturing of contaminating (DNA binding) proteins, purification, filtration or desalting.

88. The method of claim 80, wherein amplification or IV transcription comprise:
a reaction selected from the group of reactions consisting of PCR, LCR, 3SR, NASBA.

89. The method of claim 80, wherein labeling comprises:
incorporating a label into the amplified or transcribed sequence.

90. The method of claim 80, wherein labeling comprises:
labeling primers.

91. The method of claim 80, wherein labeling comprises:

incorporation of labeled dNTPs into an amplified sequence.

92. The method of claim 80, wherein labeling comprises:
covalent attachment of a particular detectable group upon the amplified sequence.

93. A method of analyzing a sample in an integrated microfluidic device having at least three chambers in fluid communication, comprising:

supplying the sample into a first chamber of the integrated microfluidic device, wherein the first chamber is selected from the group of chambers adapted to perform a preparative reaction, an analysis reaction, sample acquisition, DNA extraction, amplification, IV transcription or labeling;

performing a first reaction in the first chamber;

moving the sample from the first chamber to the second chamber, wherein the second chamber is selected from the group of chambers adapted to perform a preparative reaction, an analysis reaction, sample acquisition, DNA extraction, amplification, IV transcription or labeling;

performing a second reaction in the second chamber, the second reaction being different from the first reaction;

moving the sample from the second chamber to the third chamber, wherein the third chamber is selected from the group of chambers adapted to perform a preparative reaction, an analysis reaction, sample acquisition, DNA extraction, amplification, IV transcription or labeling;

performing a third reaction in the third chamber, the third reaction being different from both the first and second reactions;

performing confocal microscopy using a reader device

receiving a signal output from the reader device; and

analyzing the signal output with a digital computer to indicate a property of the sample.

94. The method of claim 93, wherein the preparative reaction comprises:

a reaction selected from the group of reactions consisting of sample extraction, PCR amplification, extraction of intracellular material, nucleic acid fragmentation, labeling, extension reactions and transcription reactions.

95. The method of claim 93, wherein the analysis reaction comprises:
a reaction selected from the group of reactions consisting of size based analysis or sequence based analysis.

96. The method of claim 95, wherein size based analysis comprises microcapillary electrophoresis.

97. The method of claim 95, wherein sequence based analysis comprises hybridization of targets to a nucleic acid array.

98. The method of claim 93, wherein sample acquisition reactions comprise:
a reaction selected from the group of reactions consisting of neutralizing an infectious agent or performing a pH adjustment.

99. The method of claim 98, wherein neutralizing infectious agents comprises introduction of heparin, buffering agents, protease or nuclease inhibitors or preservatives.

100. The method of claim 93, wherein DNA extraction comprises:
a reaction for extracting DNA selected from the group of reactions consisting of denaturing of contaminating (DNA binding) proteins, purification, filtration or desalting.

101. The method of claim 93, wherein amplification or IV transcription comprise:
a reaction selected from the group of reactions consisting of PCR, LCR, 3SR, NASBA.

102. The method of claim 93, wherein labeling comprises:
incorporating a label into the amplified or transcribed sequence.

103. The method of claim 93, wherein labeling comprises:
labeling primers.

104. The method of claim 93, wherein labeling comprises:
incorporation of labeled dNTPs into an amplified sequence.

105. The method of claim 93, wherein labeling comprises:
covalent attachment of a particular detectable group upon the amplified
sequence.

106. A method of analyzing a sample in an integrated microfluidic device,
comprising:

supplying the sample into a first chamber selected from the group consisting of a
chamber adapted to perform a preparative reaction, an analysis reaction, sample
acquisition, DNA extraction, amplification, IV transcription or labeling;

moving the sample from the first chamber to a second chamber by employing a
valve located in a channel between the first chamber and the second chamber, the
second chamber being selected from the group consisting of a chamber adapted to
perform a preparative reaction, an analysis reaction, sample acquisition, DNA
extraction, amplification, IV transcription or labeling; and

receiving a signal output from a reader device and indicating a property of the
sample.

107. A method of analyzing a sample in an integrated microfluidic device,
comprising:

supplying the sample into a first chamber selected from the group consisting of a
chamber adapted to perform a preparative reaction, an analysis reaction, sample
acquisition, DNA extraction, amplification, IV transcription or labeling;

moving the sample from the first chamber to a second by employing a first valve
located in a first channel between the first chamber and the second chamber, the
second chamber being selected from the group consisting of a chamber adapted to

perform a preparative reaction, an analysis reactions, sample acquisition, DNA extraction, amplification, IV transcription or labeling;

moving the sample from the second chamber to a third chamber by employing a second valve located in a second channel between the second chamber and the third chamber, the second chamber, the third chamber being selected from the group consisting of a chamber adapted to perform a preparative reaction, an analysis reactions, sample acquisition, DNA extraction, amplification, IV transcription or labeling; and

receiving a signal output from a reader device and indicating a property of the sample.

108. The method of claim 106, wherein said supplying includes placing the integrated microfluidic device in contact with a reusable base unit and supplying pressure by the reusable base unit.

109. The method of claim 107, wherein said supplying includes placing the integrated microfluidic device in contact with a reusable base unit and supplying pressure by the reusable base unit for moving the sample from the first chamber to the second chamber and for moving the sample from the second chamber to the third chamber.